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**Measles Prevention:  
Recommendations of the  
Immunization Practices  
Advisory Committee (ACIP)**

U.S. Department of Health and Human Services  
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# Measles Prevention: Recommendations of the Immunization Practices Advisory Committee (ACIP)

*These revised recommendations of the Immunization Practices Advisory Committee (ACIP) on Measles Prevention replace previous recommendations published in 1987 (1) and 1989 (2). The recommendations include a basic change in the routine childhood vaccination schedule from a one-dose to a two-dose schedule using combined measles-mumps-rubella (MMR) vaccine. Routine revaccination will generally be implemented one age group at a time starting with school enterers. New recommendations are also included for vaccination of preschool children at high risk of contracting measles, for students in colleges and other institutions of higher education, for health-care personnel and international travelers, and for outbreak control.*

## INTRODUCTION

Measles (rubeola) is often a severe disease, frequently complicated by middle ear infection or bronchopneumonia. Encephalitis occurs in approximately one of every 1,000 reported cases; survivors of this complication often have permanent brain damage and mental retardation. Death, usually from respiratory and neurologic causes, occurs in one of every 1,000 reported measles cases. The risk of death is greater for infants and adults than for children and adolescents.

Subacute sclerosing panencephalitis (SSPE) is a "slow virus" infection of the central nervous system associated with measles virus. Widespread use of measles vaccine has led to the virtual disappearance of SSPE from the United States (3).

Measles illness during pregnancy leads to increased rates of premature labor, spontaneous abortion, and low-birth-weight infants (4,5). Whether measles infection in the first trimester of pregnancy is associated with an increased rate of congenital malformations is still unresolved.

Before measles vaccine was available, more than 400,000 measles cases were reported each year in the United States (6). However, since virtually all children acquired measles, the true number of cases probably exceeded 4 million per year (i.e., the entire birth cohort). Since 1963, when both an inactivated and a live attenuated vaccine (Edmonston B strain) were licensed for use in the United States, both the type of measles vaccine and the recommended age for measles vaccination have changed several times. After 1967 and 1975, the inactivated and the Edmonston B vaccine, respectively, were no longer distributed. A live, further attenuated vaccine (Schwarz strain) was first introduced in 1965, and a similar vaccine (Moraten strain) was licensed in 1968. These further attenuated vaccines cause fewer reactions than the Edmonston B vaccine, yet are equally effective. The Moraten vaccine is the vaccine used currently in the United States.

A single dose of live measles vaccine had been recommended since measles vaccine was first licensed (1). In 1963, the recommended age for vaccination was 9 months, but in 1965 it was changed to 12 months, and in 1976 it was changed to 15 months because of evidence demonstrating greater efficacy when children were vaccinated at these ages. Persons vaccinated before the first birthday needed to be revaccinated.

## MEASLES EPIDEMIOLOGY AND ELIMINATION EFFORTS

Since vaccine licensure in 1963, the collaborative efforts of professional and voluntary medical and public health organizations in vaccination programs have resulted in a 99% reduction in the reported incidence of measles. During the late 1960s and early 1970s, the number of reported cases decreased to between 22,000 and 75,000 cases per year. Although incidence fell dramatically in all age groups, children <10 years of age showed the greatest decline, while older children had a slightly less dramatic decrease. As a result, the proportion of total cases occurring in different age groups changed. From 1984 to 1988, 58% of reported cases affected children  $\geq 10$  years of age, compared with 10% during the period 1960 to 1964 (6).

In 1978, the Department of Health, Education, and Welfare initiated a Measles Elimination Program, with a goal to eliminate indigenous measles from the United States by October 1, 1982. The three components of this program have been 1) maintenance of high levels of immunity, 2) careful surveillance of disease, and 3) aggressive outbreak control. As a result of these efforts, the number of cases reported annually dropped from 26,871 in 1978 to an all-time low of 1,497 in 1983. The number of cases reported then increased until 1986 (6,282) cases (7). Reported cases decreased in 1987 and 1988 but rose again during the first 48 weeks of 1989, when more than 14,000 cases were reported.

Measles cases are routinely reported by state and local health departments to the *MMWR*. The Division of Immunization, Center for Prevention Services, CDC, collects supplementary data on cases, including information on vaccination status (i.e., vaccinated or unvaccinated). Persons appropriately vaccinated for measles are those who have received a dose of live measles vaccine on or after their first birthday.

Unvaccinated persons with measles can be subclassified into three general groups: those for whom vaccine is not routinely indicated (e.g., those <16 months of age, born before 1957, with prior physician diagnosis of measles, or with medical contraindications), those for whom vaccination is difficult to achieve (e.g., non-U.S. citizens and persons exempted for religious or philosophic reasons), and those for whom vaccine is indicated (e.g., children  $\geq 16$  months of age and children vaccinated before their first birthdays). From 1985 through 1988, information on vaccination status for 16,819 measles cases was collected by the Division of Immunization. Appropriately vaccinated persons accounted for 42%, and 92% of cases in this group occurred among persons  $\geq 5$  years of age. In 26% of these cases, the patients were unvaccinated persons for whom vaccine was not routinely indicated or for whom vaccination was difficult to achieve. The remaining 32% were unvaccinated persons for whom vaccine was indicated. Forty-two percent of the persons in this latter group were children 16 months to 4 years of age.

In recent years, two major types of outbreaks have occurred in the United States: those among unvaccinated preschool-aged children, including those younger than

the recommended age for vaccination (i.e., <15 months), and those among vaccinated school-aged children (8). In addition, particularly in 1989, a substantial number of cases occurred among students and personnel on college campuses. Large outbreaks occurred among unvaccinated preschool-aged children in several inner-city areas. In these outbreaks, of the cases that occurred among vaccine-eligible children 16 months-4 years of age, up to 88% of the children were unvaccinated. As many as 40% of cases occurred among children <16 months of age. In some of these areas, surveys indicate that 49%-65% of 2-year-olds had received measles vaccine (9). Among school-aged children, outbreaks have occurred in schools with vaccination levels of >98%. These outbreaks have occurred in all parts of the country, including areas that had not reported measles for years.

In general, attack rates in individual schools were low (1%-5%) and the calculated vaccine efficacy high. Most of the persons with measles in college outbreaks were also likely to have been vaccinated, although documentation of vaccination was often lacking. However, in many outbreaks, children vaccinated at 12-14 months of age had higher attack rates than those vaccinated at older ages (10). In a few outbreaks, older persons vaccinated in the more distant past were at increased risk for disease; this risk was independent of age at vaccination (11).

The goal of eliminating measles in the United States has not been reached primarily because of 1) failure to implement the current vaccination strategy, resulting in large numbers of unvaccinated preschool-age children in some areas, and 2) vaccine failure. A substantial number of cases occur among persons who previously have been vaccinated. Theoretically, vaccine failures may either be primary (i.e., an adequate response to vaccination never developed) or secondary (i.e., an adequate response initially developed, but immunity was lost over time). Some of the reported vaccine failures may be explained by the fact that a person's records incorrectly indicated appropriate vaccination. Measles vaccine is at least 95% effective for children vaccinated at  $\geq 15$  months of age. However, efficacy may be slightly lower for persons vaccinated between 12 and 14 months of age, presumably because transplacental maternal antibody persists beyond the first birthday in some children and interferes with the response to vaccination. Also, secondary vaccine failure could occur after successful vaccination as a result of waning immunity, but the percentage of persons to whom this applies appears to be small (12,13). Overall, the great majority of vaccinees appear to have long-term and probably life-long immunity. Nevertheless, further studies are needed to determine the duration of vaccine-induced immunity.

## CHANGES IN MEASLES VACCINATION POLICY

The Committee reviewed current measles epidemiology and the measles elimination strategy and considered modifications. New recommendations were developed to help achieve the goal of measles elimination (Tables 1 and 2). A routine two-dose measles vaccination schedule now is recommended. This schedule is expected to provide protection to most persons who do not respond to their initial vaccination.

The first dose is recommended at 15 months of age for children in most areas of the country but at 12 months of age for children in some areas with recurrent measles transmission. The second dose is recommended at the time a child enters school at

kindergarten or first grade (see "Vaccine Usage"). Because programs to administer a second dose of measles vaccine at school entry to kindergarten or first grade will not have an immediate effect on the incidence of measles for school-aged children, programs also are recommended for outbreak control (see "Outbreak Control") and for the routine vaccination of students entering college (see "Special Situations").

When fully implemented, this schedule should lead to the elimination of measles among school-aged children and college students. It is expected to prevent the 35%-40% of cases affecting persons  $\geq 5$  years of age who appear to be vaccine failures, and it may indirectly protect unvaccinated persons since the risk of exposure to measles will decrease. Outbreaks of measles in school settings are likely to cease, thus avoiding the substantial disruption of routine activities and the high cost of outbreak control. However, the overall goal of eliminating measles in the United States also requires more intensive efforts to vaccinate preschool children at the recommended ages, particularly children residing in inner cities.

All contacts with health-care providers in physicians' offices, clinics, emergency rooms, and hospitals are opportunities for evaluating the vaccination status of children, both patients and accompanying siblings, and for offering vaccine to those who need it. Unvaccinated children should not be rescheduled for vaccination; rather, they should be vaccinated immediately if no contraindication exists. Particular attention should be paid to offering simultaneous vaccination. No preschool child

**TABLE 1. 1989 Recommendations for measles vaccination**

Routine childhood schedule, United States

Most areas	Two doses* <sup>†</sup> -first dose at 15 months -second dose at 4-6 years (entry to kindergarten or first grade) <sup>§</sup>
High-risk areas <sup>¶</sup>	Two doses* <sup>†</sup> -first dose at 12 months -second dose at 4-6 years (entry to kindergarten or first grade) <sup>§</sup>
Colleges and other educational institutions post-high school	Documentation of receipt of two doses of measles vaccine after the first birthday <sup>†</sup> or other evidence of measles immunity**.
Medical personnel beginning employment	Documentation of receipt of two doses of measles vaccine after the first birthday <sup>†</sup> or other evidence of measles immunity**.

\*Both doses should preferably be given as combined measles, mumps, rubella vaccine (MMR).

<sup>†</sup>No less than 1 month apart. If no documentation of any dose of vaccine, vaccine should be given at the time of school entry or employment and no less than 1 month later.

<sup>§</sup>Some areas may elect to administer the second dose at an older age or to multiple age groups (see "Age at Vaccination").

<sup>¶</sup>A county with more than five cases among preschool-aged children during each of the last 5 years, a county with a recent outbreak among unvaccinated preschool-aged children, or a county with a large inner-city urban population. These recommendations may be applied to an entire county or to identified risk areas within a county.

\*\*Prior physician-diagnosed measles disease, laboratory evidence of measles immunity, or birth before 1957.

who needs MMR should be offered other vaccines without being offered MMR. Special efforts are also needed to educate and motivate parents to have such children vaccinated.

## MEASLES VIRUS VACCINE

Live measles virus vaccine\* used in the United States is prepared in chick-embryo-cell culture. It is available in monovalent (measles only) form and in two combinations: measles-rubella (MR) and measles-mumps-rubella (MMR) vaccines†.

Measles vaccine produces an inapparent or mild, noncommunicable infection. Measles antibodies develop in at least 95% of susceptible children vaccinated at  $\geq 15$  months of age. Although the titers of vaccine-induced antibodies are lower than those

\*Official name: Measles Virus Vaccine, Live Attenuated.

†Available in the United States as Attenuvax® (single antigen), M-R-Vax® (measles-rubella) and M-M-R II® (measles-mumps-rubella), from the Merck, Sharp and Dohme Co.

**TABLE 2. Recommendations for measles outbreak control\***

Outbreaks in preschool-aged children	Lower age for vaccination to as low as 6 months of age in outbreak area if cases are occurring in children <1 year of age†.
Outbreaks in institutions: day-care centers, K-12th grades, colleges, and other institutions	Revaccination of all students and their siblings and of school personnel born in or after 1957 who do not have documentation of immunity to measles‡.
Outbreaks in medical facilities	<p>Revaccination of all medical workers born in or after 1957 who have direct patient contact and who do not have proof of immunity to measles‡. Vaccination may also be considered for workers born before 1957.</p> <p>Susceptible personnel who have been exposed should be relieved from direct patient contact from the 5th to the 21st day after exposure (regardless of whether they received measles vaccine or IG) or—if they become ill—for 7 days after they develop rash.</p>

\*Mass revaccination of entire populations is not necessary. Revaccination should be limited to populations at risk, such as students attending institutions where cases occur.

†Children initially vaccinated before the first birthday should be revaccinated at 15 months of age. A second dose should be administered at the time of school entry or according to local policy.

‡Documentation of physician-diagnosed measles disease, serologic evidence of immunity to measles, or documentation of receipt of two doses of measles vaccine on or after the first birthday.

following natural disease, both serologic and epidemiologic evidence indicate that vaccine-induced protection appears to be long-lasting in most individuals.

### **Vaccine Shipment and Storage**

The administration of improperly stored vaccine may fail to provide protection against measles. Although the current measles vaccine may be more thermostable than vaccine produced in the past, it should be stored at 2-8 C (35.6-46.4 F) or colder during storage. Vaccine must be shipped at 10 C (50 F) or colder and may be shipped on dry ice. It must be protected from light, which may inactivate the virus. Reconstituted vaccine must be stored in a refrigerator (not frozen) and discarded if not used within 8 hours.

## **VACCINE USAGE**

### **General Recommendations**

All vaccines containing measles virus are recommended for routine use for children 15 months of age. Persons born in or after 1957 who lack documentation of measles immunity (see "Measles Immunity") are considered susceptible and should be vaccinated if there are no contraindications (see "Precautions and Contraindications"). All vaccinations should be documented in the patient's permanent medical record (14). A parental history of vaccination, by itself, is not considered adequate documentation. A physician should not provide an immunization record for a patient unless s/he has administered the vaccine or has seen a record that documents vaccination. Most persons born before 1957 are likely to have been naturally infected with measles virus and generally need not be considered susceptible; however, vaccination may be offered to these persons if there is reason to believe they may be susceptible.

Both doses of measles vaccine should be given as combined MMR vaccine when given on or after the first birthday. The combined vaccine is preferred to assure immunity to all three viruses. Mumps revaccination is particularly important. Recent studies have shown that mumps can occur in highly vaccinated populations, resulting in substantial numbers of cases among persons with histories of prior mumps vaccination. Although rubella vaccine failure has not been a major problem, the potential consequences of rubella vaccine failure are substantial (i.e., congenital rubella syndrome), and the use of MMR should provide an additional safeguard against such failures.

The most commonly used laboratory test for assessing immunity to measles has been the hemagglutination-inhibition (HI) test. Other more sensitive assays, such as the enzyme immuno-assay (EIA), are now being used by many laboratories. Persons with measles-specific antibody, detectable by any test, are considered immune. Routine serologic screening to determine measles immunity is not generally recommended, although it may be cost-effective in some situations (e.g., large prepaid medical programs). However, the test may not be widely available, and screening requires that tracking systems be established to assure that identified susceptibles return for vaccination. In addition, screening for antibodies for mumps and rubella would further decrease the cost-effectiveness of this strategy.

## **Dosage**

Two doses of measles vaccine, generally given as MMR, are recommended for all children after the first birthday. The dose is 0.5 ml and should be given subcutaneously.

## **Age at Vaccination**

### **Routine childhood immunization schedule for most areas of the United States**

The first dose of measles vaccine should be given when children are  $\geq 15$  months of age. The second dose should routinely be given when children enter kindergarten or first grade (4-6 years of age).

The recommended time for the second dose is based primarily on administrative considerations. The current childhood immunization schedule recommends other vaccines (diphtheria and tetanus toxoids and pertussis vaccine [DTP] and oral poliovirus vaccine [OPV]) when children enter school; therefore, an additional provider visit for the second dose of measles vaccine is not necessary. In addition, most school authorities have systems at this grade level for identifying and tracking children with incomplete immunizations.

Because many of the vaccine failures in recent outbreaks of measles have occurred among 10 to 19-year-old children and adolescents, administering the second dose at the time of school entry may not achieve full impact on the incidence of measles for 5 to 15 years. For the impact to occur more rapidly, some localities may choose to give students the second dose at an older age (e.g., when they enter middle school or junior high school). In deciding when to administer the second dose, health officials should consider how they can best achieve a high vaccination rate since this is essential to assure maximum impact of a two-dose schedule. Some localities may want to provide a second dose to multiple age groups from kindergarten through 12th grade to achieve complete immunization of all school-aged children more rapidly.

Children who have received two doses of live measles vaccine on or after the first birthday (at least 1 month apart) do not need an additional dose when they enter school. Children who have no documentation of live measles vaccination when they enter school should be admitted after the first dose. A second dose should be given according to local policy, but no less than 1 month later.

### **Routine childhood immunization schedule for areas with recurrent measles transmission**

Initial vaccination with MMR at 12 months of age is recommended for children living in high-risk areas. This strategy assumes that the benefit of preventing measles cases between 12 and 15 months of age outweighs the slightly lower efficacy of the vaccine when given at this age. A high-risk area is defined as: 1) a county with more than five cases among preschool-aged children during each of the last 5 years, 2) a county with a recent outbreak among unvaccinated preschool-aged children, or 3) a county with a large inner-city urban population. These recommendations may be implemented for an entire county or only in defined high-risk areas.

## Revaccination of Persons Vaccinated According to Earlier Recommendations

### Previous vaccination with live vaccine

Persons vaccinated with live measles vaccine before their first birthday should be considered unvaccinated. If they are entering kindergarten or first grade, college or other post-high school educational institutions (see "Special Situations"), or beginning employment in a medical facility (see "Special Situations") and cannot provide documentation of immunity to measles (see "Measles Immunity"), they should receive two doses of vaccine no less than 1 month apart.

Live attenuated Edmonston B vaccine (distributed from 1963-1975) was usually administered with immune globulin (IG) or high-titer measles immune globulin (MIG; no longer available in the United States). This vaccine, administered on or after the first birthday, is acceptable as an effective first dose of vaccine. A second dose should be administered as recommended above. However, if a further attenuated measles vaccine (i.e., Schwarz or Moraten) was given simultaneously with IG or MIG, the IG or MIG may have impaired the immune response to vaccination. Persons who received measles vaccine of unknown type or further attenuated measles vaccine accompanied by IG or MIG should be considered unvaccinated and should be given two doses of vaccine as outlined above.

### Previous vaccination with inactivated vaccine or vaccine of unknown type

Inactivated (killed) measles vaccine was available in the United States only from 1963 to 1967 but was available through the early 1970s in some other countries. It was frequently given as a series of two or three injections. Some persons who received inactivated vaccine are at risk of developing severe atypical measles syndrome when exposed to the natural virus (15). Consequently, such persons should receive two doses of live vaccine separated by no less than 1 month. Persons vaccinated with inactivated vaccine followed within 3 months by live vaccine should be revaccinated with two doses of live vaccine. Revaccination is particularly important when the risk of exposure to natural measles virus is increased, as may occur during international travel.

A wide range (4%-55%) of recipients of inactivated measles vaccine who were later revaccinated with live measles vaccine have had reactions to the live vaccine (16). Most of these reactions have been mild, consisting of local swelling and erythema, with or without low-grade fever lasting 1-2 days. Rarely, more severe reactions, including prolonged high fevers and extensive local reactions, have been reported. However, recipients of inactivated measles vaccine are more likely to have serious illness when exposed to natural measles than when given live measles virus vaccine.

These same recommendations for revaccination apply to persons vaccinated between 1963 and 1967 with vaccine of unknown type, since they may have received inactivated vaccine. Since inactivated measles vaccine was not distributed in the United States after 1967, persons vaccinated after 1967 with a vaccine of unknown type need not be revaccinated routinely unless the original vaccination occurred before the first birthday or was accompanied by IG or MIG. However, such persons should receive a second dose if they are entering college, beginning employment in medical facilities, or planning international travel.

## Measles Immunity

Persons are considered immune to measles if they 1) were born before 1957, 2) have documentation of physician-diagnosed measles, 3) have laboratory evidence of immunity to measles, or 4) have documentation of adequate vaccination. Eventually, adequate vaccination will be defined as receipt of one dose of live measles vaccine on or after the first birthday for children before they enter school and two doses of measles vaccine on or after the first birthday for children who are entering or have entered school.

For localities implementing the second dose for students at ages beyond school entry (e.g., entry to middle school or junior high school), acceptable evidence of immunity will be one dose at school entry and two doses for students older than the routine age of the second dose (see "Age at Vaccination").

Since most areas will implement the two-dose schedule one age group at a time, criteria for adequate vaccination will vary in the interim. For example, if the two-dose schedule is implemented in 1990, children in kindergarten or first grade will need to have documentation of two doses of measles vaccine after the first birthday to be considered adequately vaccinated. However, a single dose of vaccine will be acceptable evidence of adequate vaccination for children in higher grades. Two years later, children in kindergarten through second or third grade will need two doses of measles vaccine for acceptable evidence of adequate vaccination. Similar criteria would apply if the second-dose strategy is implemented at an older age (see "Age at Vaccination").

The interim vaccination criteria for adequate measles vaccination noted above apply to routine settings only. During outbreaks, all persons at risk and born in or after 1957 who are in kindergarten, first grade, or beyond will need two doses on or after the first birthday as evidence of adequate vaccination (see "Outbreak Control").

## Individuals Exposed to Disease

### Use of vaccine

Exposure to measles is not a contraindication to vaccination. If live measles vaccine is given within 72 hours of measles exposure, it may provide some protection. This approach is preferable to using IG for persons  $\geq 12$  months of age. If the exposure does not result in infection, vaccination should induce protection against subsequent measles infection.

### Use of IG

IG can prevent or modify measles in a susceptible person if given within 6 days of exposure. The recommended dose of IG is 0.25 ml/kg (0.11 ml/lb) of body weight (maximum dose = 15 ml). IG may be especially indicated for susceptible household contacts of measles patients, particularly contacts  $< 1$  year of age, pregnant women, or immunocompromised persons, for whom the risk of complications is increased. The recommended dose of IG for immunocompromised persons is 0.5 ml/kg of body weight (maximum dose = 15 ml). Live measles vaccine should be given 3 months later (when passively acquired measles antibodies should have disappeared) if the individual is then at least 15 months old. IG should not be used to control measles outbreaks.

## Special Situations

### Recommendations for colleges and other institutions

Colleges, technical schools, and other institutions for post-high school education should require documentation of two doses of live measles-containing vaccines, documentation of prior physician-diagnosed measles disease, or laboratory evidence of measles immunity before entry for all students born in or after 1957. Students who have no documentation of live measles vaccination or other evidence of measles immunity at the time of school entry should be admitted after receiving the first dose. A second dose should be given no less than 1 month later. Institutions may wish to extend this requirement to all classes.

### Recommendations for medical facilities

Medical personnel are at higher risk for acquiring measles than the general population (17). Hospitals should require evidence of two live measles vaccinations, documentation of physician-diagnosed measles disease, or laboratory evidence of measles immunity for medical staff beginning employment who will have direct patient contact. Persons born in or after 1957 who have no documentation of vaccination or other evidence of measles immunity should be vaccinated at the time of employment and revaccinated no less than 1 month later. If resources are available, institutions may wish to extend this recommendation to all medical personnel, not just those beginning employment. Since some medical personnel who have acquired measles in medical facilities were born before 1957, institutions may consider requiring at least one dose of measles vaccine for older employees who are at risk of occupational exposure to measles.

### Recommendations for international travel

Persons traveling abroad should be immune to measles. The protection of young adults who have escaped measles disease and have not been vaccinated is especially important. Consideration should be given to providing a dose of measles vaccine to persons born in or after 1957 who travel abroad, who have not previously received two doses of measles vaccine, and who do not have other evidence of measles immunity (see "Measles Immunity").

The age for measles vaccination should be lowered for children traveling to areas in which measles is endemic or epidemic. Children 12-14 months of age should receive MMR vaccine before their departure. Children 6-11 months of age should receive a dose of monovalent measles vaccine before departure, although there is no specific contraindication to the use of MMR for this age group if monovalent measles vaccine is not available. Seroconversion rates observed for measles, mumps, and rubella antigens are significantly less among children vaccinated before the first birthday than among older children. Children who receive monovalent measles vaccine or MMR before their first birthday should be considered unvaccinated and should receive two doses of MMR at later ages. Whereas the optimal age for the first revaccination dose is 15 months, the age for revaccination may be as low as 12 months if the child remains in a high-risk area (see "Routine childhood immunization schedule for areas with recurrent measles transmission"). The second revaccination dose would normally be given when a child enters school or according to local policy.

Since virtually all infants <6 months of age will be protected by maternally derived antibodies, no additional protection against measles is necessary in this age group.

## **SIDE EFFECTS AND ADVERSE REACTIONS**

More than 170 million doses of measles vaccine were distributed in the United States from 1963 through 1988. The vaccine has an excellent record of safety. From 5%-15% of vaccinees may develop a temperature of  $\geq 103$  F ( $\geq 39.4$  C) beginning 5-12 days after vaccination and usually lasting several days (18). Most persons with fever are otherwise asymptomatic. Transient rashes have been reported for approximately 5% of vaccinees. Central nervous system conditions, including encephalitis and encephalopathy, have been reported with a frequency of less than one per million doses administered. The incidence of encephalitis or encephalopathy after measles vaccination of healthy children is lower than the observed incidence of encephalitis of unknown etiology. This finding suggests that the reported severe neurologic disorders temporally associated with measles vaccination were not caused by the vaccine. These adverse events should be anticipated only in susceptible vaccinees and do not appear to be age-related. After revaccination, reactions should be expected to occur only among the small proportion of persons who failed to respond to the first dose.

### **Personal and Family History of Convulsions**

As with the administration of any agent that can produce fever, some children may have a febrile seizure. Although children with a personal or family history of seizures are at increased risk for developing idiopathic epilepsy, febrile seizures following vaccinations do not in themselves increase the probability of subsequent epilepsy or other neurologic disorders. Most convulsions following measles vaccination are simple febrile seizures, and they affect children without known risk factors.

An increased risk of these convulsions may occur among children with a prior history of convulsions or those with a history of convulsions in first-degree family members (i.e., siblings or parents) (19). Although the precise risk cannot be determined, it appears to be low.

In developing vaccination recommendations for these children, the Committee considered a number of factors, including risks from measles disease, the large proportion (5%-7%) of children with a personal or family history of convulsions, and the fact that convulsions following measles vaccine are uncommon and have not been associated with permanent brain damage. The Committee concluded that the benefits of vaccinating these children greatly outweigh the risks. They should be vaccinated just as children without such histories.

Because the period for developing vaccine-induced fever occurs approximately 5-12 days after vaccination, prevention of febrile seizures is difficult. Prophylaxis with antipyretics is one alternative, but these agents may not be effective if given after the onset of fever. They would have to be initiated before the expected onset of fever and continued for 5-7 days. However, parents should be alert to the occurrence of fever after vaccination and should treat their children appropriately.

Children who are being treated with anticonvulsants should continue to take them after measles vaccination. Because protective levels of most currently available anticonvulsant drugs (e.g., phenobarbital) are not achieved for some time after therapy is initiated, prophylactic use of these drugs does not seem feasible.

The parents of children who have either a personal or family history of seizures should be advised of the small increased risk of seizures following measles vaccination. In particular, they should be told in advance what to do in the unlikely event that a seizure occurs. The permanent medical record should document that the small risk of postimmunization seizures and the benefits of vaccination have been discussed.

### **Revaccination Risks**

There is no evidence of increased risk from live measles vaccination in persons who are already immune to measles, as a result of either previous vaccination or natural disease.

## **PRECAUTIONS AND CONTRAINDICATIONS**

### **Pregnancy**

Live measles vaccine, when given as a component of MR or MMR, should not be given to women known to be pregnant or who are considering becoming pregnant within the next 3 months. Women who are given monovalent measles vaccine should not become pregnant for at least 30 days after vaccination. This precaution is based on the theoretical risk of fetal infection, although no evidence substantiates this theoretical risk. Considering the importance of protecting adolescents and young adults against measles, asking women if they are pregnant, excluding those who are, and explaining the theoretical risks to the others before vaccination are sufficient precautions.

### **Febrile Illness**

The decision to administer or delay vaccination because of a current or recent febrile illness depends largely on the cause of the illness and the severity of symptoms. Minor illnesses, such as a mild upper-respiratory infection with or without low-grade fever, are not contraindications for vaccination. For persons whose compliance with medical care cannot be assured, every opportunity should be taken to provide appropriate vaccinations.

Children with moderate or severe febrile illnesses can be vaccinated as soon as they have recovered. This wait avoids superimposing adverse effects of vaccination on the underlying illness or mistakenly attributing a manifestation of the underlying illness to the vaccine. Performing routine physical examinations or measuring temperatures are not prerequisites for vaccinating infants and children who appear to be in good health. Asking the parent or guardian if the child is ill, postponing vaccination for children with moderate or severe febrile illnesses, and vaccinating those without contraindications are appropriate procedures in childhood immunization programs.

### **Allergies**

Hypersensitivity reactions following the administration of live measles vaccine are rare. Most of these reactions are minor and consist of a wheal and flare or urticaria at

the injection site. More than 170 million doses of measles vaccine have been distributed in the United States, but only five reported cases of immediate allergic reactions have occurred among children who had histories of anaphylactic reactions to egg ingestion. These reactions could potentially have been life threatening. Four children experienced difficulty in breathing, and one of these four had hypotension. Persons with a history of anaphylactic reactions (hives, swelling of the mouth and throat, difficulty in breathing, hypotension, and shock) following egg ingestion should be vaccinated only with extreme caution. Protocols have been developed for vaccinating such persons (20,21). However, persons are not at increased risk if they have egg allergies that are not anaphylactic in nature; they can be vaccinated in the usual manner. Persons with allergies only to chickens or feathers are not at increased risk of reaction to measles vaccination.

MMR vaccine and its component vaccines contain trace amounts of neomycin. Although the amount present is less than that usually used for a skin test to determine hypersensitivity, persons who have experienced anaphylactic reactions to neomycin should not be given these vaccines. Most often, neomycin allergy is manifested by contact dermatitis rather than anaphylaxis. A history of contact dermatitis to neomycin is not a contraindication to receiving measles vaccine. Live measles virus vaccine does not contain penicillin.

### **Recent Administration of IG**

Vaccine virus replication and stimulation of immunity usually occurs 1-2 weeks after vaccination. When the live measles vaccine is given after IG or specific IG preparations, the vaccine virus might not replicate successfully, and the antibody response could be diminished. Measles vaccine should not be given for at least 6 weeks, and preferably for 3 months, after a person has been given IG, whole blood, or other antibody-containing blood products. If vaccine is given to a person who has received such products within the preceding 3 months, the dose should not be counted and the person should be revaccinated approximately 3 months later unless serologic testing indicates that measles-specific antibodies have been produced. For international travelers, measles vaccination should precede the administration of IG by at least 2 weeks to preclude interference with replication of the vaccine virus. If the interval between measles vaccination and subsequent administration of an IG preparation is <14 days, vaccination should be repeated 3 months later, unless serologic testing indicates that antibodies were produced.

### **Tuberculosis**

Tuberculosis may be exacerbated by natural measles infection. Live measles virus vaccine has not been shown to have such an effect. Tuberculin skin testing is not a prerequisite for measles vaccination. If tuberculin testing is needed for other reasons, it can be done the day of vaccination. Otherwise, the test should be postponed for 4-6 weeks, since measles vaccination may temporarily suppress tuberculin reactivity.

### **Altered Immunocompetence**

Replication of vaccine viruses can be enhanced in persons with immune-deficiency diseases and in persons with immunosuppression, as occurs with leukemia, lymphoma, generalized malignancy, or therapy with alkylating agents, antimetabolites,

radiation, or large doses of corticosteroids. For this reason, patients with such conditions or therapies (except patients with symptomatic infection with human immunodeficiency virus [HIV]; see below) should not be given live measles virus vaccine.

Patients with leukemia in remission who have not received chemotherapy for at least 3 months may receive live-virus vaccines. Short-term (<2 weeks), low- to moderate-dose systemic corticosteroid therapy, topical steroid therapy (e.g., nasal, skin), long-term alternate-day treatment with low to moderate doses of short-acting systemic steroids, and intra-articular, bursal, or tendon injection of corticosteroids are not immunosuppressive in their usual doses and do not contraindicate the administration of measles vaccine.

The growing number of infants and preschoolers with HIV infection has directed special attention to the appropriate immunization of such children. Asymptomatic children do not need to be evaluated and tested for HIV infection before decisions concerning vaccination are made. Asymptomatic HIV-infected persons in need of MMR should receive it. MMR should be considered for all symptomatic HIV-infected children, including children with acquired immunodeficiency syndrome (AIDS), since measles disease in these children can be severe. Limited data on MMR vaccination among both asymptomatic and symptomatic HIV-infected children indicate that MMR has not been associated with severe or unusual adverse events, although antibody responses have been unpredictable (22-24).

The administration of high-dose intravenous immune globulin (IGIV) at regular intervals to HIV-infected children is being studied to determine whether it will prevent a variety of infections. MMR vaccine may be ineffective if it is administered to a child who has received IGIV during the preceding 3 months.

### **Management of Patients with Contraindications to Measles Vaccine**

If immediate protection against measles is required for persons with contraindications to measles vaccination, passive immunization with IG, 0.25 ml/kg (0.11 ml/lb) of body weight (maximum dose = 15 ml), should be given as soon as possible after known exposure. Exposed symptomatic HIV-infected and other immunocompromised persons should receive IG regardless of their previous vaccination status; however, IG in usual doses may not be effective in such patients. For immunocompromised persons, the recommended dose is 0.5 ml/kg of body weight if IG is administered intramuscularly (maximum dose = 15 ml). This corresponds to a dose of protein of approximately 82.5 mg/kg (maximum dose = 2,475 mg). Intramuscular IG may not be needed if a patient with HIV infection is receiving 100-400 mg/kg IGIV at regular intervals and the last dose was given within 3 weeks of exposure to measles. Because the amounts of protein administered are similar, high-dose IGIV may be as effective as IG given intramuscularly. However, no data are available concerning the effectiveness of IGIV in preventing measles.

### **Simultaneous Administration of Vaccines**

In general, simultaneous administration of the most widely used live and inactivated vaccines does not impair antibody responses or increase rates of adverse reactions (25). The administration of MMR vaccine yields results similar to the administration of individual measles, mumps, and rubella vaccines at different sites or at different times.

There are equivalent antibody responses and no clinically significant increases in the frequency of adverse events when DTP, MMR, and OPV or inactivated poliovirus vaccine (IPV) are administered either simultaneously at different sites or at separate times. Routine simultaneous administration of MMR, DTP, and OPV (or IPV) is recommended for all children  $\geq 15$  months of age who are eligible to receive these vaccines. Vaccination with MMR at 15 months followed by DTP, OPV (or IPV), and *Haemophilus influenzae* b conjugate vaccine (HbCV) at 18 months remains an acceptable alternative for children with caregivers known to be generally compliant with other health-care recommendations. No data are available on the concomitant administration of HbCV or *H. influenzae* b polysaccharide vaccine (HbPV) and OPV and MMR vaccine. If the child might not be brought back for future vaccinations, the simultaneous administration of all vaccines (including DTP, OPV, MMR, and HbCV or HbPV) is recommended, as appropriate to the recipient's age and previous vaccination status.

## OUTBREAK CONTROL

All reports of suspected measles cases should be investigated promptly. A measles outbreak exists in a community whenever one case of measles is confirmed. Once this occurs, preventing the dissemination of measles depends on the prompt vaccination of susceptible persons. Control activities should not be delayed for laboratory results on suspected cases. Persons who cannot readily provide documentation of measles immunity (see "Measles Immunity") should be vaccinated or excluded from the setting (e.g., school). Documentation of vaccination is adequate only if the date of vaccination is provided. Almost all persons who are excluded from an outbreak area because they lack documentation of immunity quickly comply with vaccination requirements. Persons who have been exempted from measles vaccination for medical, religious, or other reasons should be excluded from the outbreak area until at least 2 weeks after the onset of rash in the last case of measles.

### School-based Outbreaks

During outbreaks in day-care centers; elementary, middle, junior, and senior high schools; and colleges and other institutions of higher education, a program of revaccination with MMR vaccine is recommended in the affected schools. Consideration should be given to revaccination in unaffected schools that may be at risk of measles transmission. Revaccination should include all students and their siblings and all school personnel born in or after 1957 who cannot provide documentation that they received two doses of measles-containing vaccine on or after their first birthday or other evidence of measles immunity (see "Measles Immunity"). Persons revaccinated, as well as unvaccinated persons receiving their first dose as part of the outbreak control program, may be immediately readmitted to school. Mass revaccination of entire communities is not necessary.

### Quarantine

Imposing quarantine measures for outbreak control is both difficult and disruptive to schools and other organizations. Under special circumstances restriction of an event might be warranted; however, such action is not recommended as a routine measure for outbreak control.

## Outbreaks Among Preschool-aged Children

The risk of complications from measles is high among infants <1 year of age. Therefore, considering the benefits and risks, vaccination with monovalent measles vaccine is recommended for infants as young as 6 months of age when exposure to natural measles is considered likely. MMR may be administered to children before the first birthday if monovalent measles vaccine is not readily available. Children vaccinated before the first birthday should be revaccinated when they are 15 months old and when they enter school to ensure adequate protection (see "General Recommendations").

### Medical Settings

If an outbreak occurs in the areas served by a hospital or within a hospital, all employees with direct patient contact who were born in or after 1957 who cannot provide documentation they they received two doses of measles vaccine on or after their first birthday or other evidence of immunity to measles (see "Measles Immunity") should receive a dose of measles vaccine. Since some medical personnel who have acquired measles in medical facilities were born before 1957, vaccination of older employees who may have occupational exposure to measles should also be considered during outbreaks. Susceptible personnel who have been exposed should be relieved from direct patient contact from the fifth to the 21st day after exposure regardless of whether they received vaccine or IG after the exposure. Personnel who become ill should be relieved from patient contact for 7 days after they develop rash.

## DISEASE SURVEILLANCE AND REPORTING OF ADVERSE EVENTS

### Disease Surveillance

As the incidence of measles declines in the United States, aggressive surveillance becomes increasingly important. Effective surveillance can delineate inadequate levels of protection, define groups needing special attention, and assess the effectiveness of control activities.

Known or suspected measles cases should be reported immediately to local health departments. Serologic confirmation should be attempted for every suspected case of measles that cannot be linked to a confirmed case. Reporting of suspected cases and implementation of outbreak-control activities should not be delayed pending laboratory results.

The traditional serologic diagnosis of measles requires a significant rise in antibody titer between acute- and convalescent-phase sera. However, the diagnosis can also be made by demonstrating the presence of IgM antibody in a single specimen. Correct interpretation of serologic data depends upon the proper timing of specimen collection in relation to rash onset. This timing is especially important for interpreting negative IgM results, since IgM antibody peaks approximately 10 days after rash onset and is usually undetectable 30 days after rash onset.

Asymptomatic reinfection can occur in persons who have previously developed antibodies, whether from vaccination or from natural disease. Symptomatic reinfections are rare. These reinfections have been accompanied by rises in measles antibody titers.

## Reporting of Adverse Events

The National Childhood Vaccine Injury Act of 1986 requires physicians and other health care providers who administer vaccines to maintain permanent immunization records and to report occurrences of adverse events specified in the Act (14). These adverse events, as well as other adverse events that require medical attention, must be reported to the U.S. Department of Health and Human Services. Although there eventually will be one system for reporting adverse events following immunizations, two separate systems currently exist. The appropriate reporting method depends on the source of funding used to purchase the vaccine. If a vaccine was purchased with public funds, adverse events should be reported to the appropriate local, county, or state health department. The state health department submits its report to CDC. If vaccine was purchased with private money, adverse events should be reported directly to the Food and Drug Administration.

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